PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference | FOR FURTHER | | see Form PCT/ISA/220 | |
|--|---|----------------------|---|--|
| AX02A02/P-WO | ACTION as we | | Il as, where applicable, item 5 below. | |
| International application No. | International filing date (day/monti | h∕year) | (Earliest) Priority Date (day/month/year) | |
| PCT/EP2004/006698 | 21/06/2004 | | 20/06/2003 | |
| Applicant | | | <u> </u> | |
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| AXIOGENESIS AG | | | | |
| This International Search Report has been | nranged by this International Con- | abias Aust | | |
| according to Article 18. A copy is being tra | insmitted to the International Bureau | · | forty and is transmitted to the applicant | |
| This International Search Report consists | of a total of 5he | ets. | | |
| | a copy of each prior art document ci | | report. | |
| | | | | |
| Basis of the report a. With regard to the language, the in | ntemational search was carried out | an tha hac | is of the international application in the | |
| language in which it was filed, unle | ess otherwise indicated under this ite | m. | is of the international application in the | |
| The international s | earch was carried out on the basis o | of a transla | tion of the international application furnished to | |
| ans Addionly (Adie | e 23.1(D)). | | | |
| b. With regard to any nucleo | tide and/or amino acid sequence of | disclosed in | n the international application, see Box No. 1. | |
| 2. X Certain claims were foun | d unsearchable (See Box II). | | | |
| | | | | |
| 3. Unity of invention is lack | ing (see Box III). | | | |
| 4. With regard to the title, | | | | |
| X the text is approved as sub | mitted by the applicant. | | | |
| the text has been established | ed by this Authority to read as follow | s: | | |
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| . With regard to the abstract, | | | | |
| the text is approved as subm | | | | |
| may, within one month from | d, according to Rule 38.2(b), by this the date of mailing of this internation | Authority and search | as it appears in Box No. IV. The applicant report, submit comments to this Authority. | |
| . With regard to the drawings, | | | • | |
| a. the figure of the drawings to be pub | lished with the abstract is Figure No. | | • | |
| as suggested by the | | | | |
| = | authority, because the applicant failed | d to sunne | st a figure. | |
| _ | authority, because this figure better c | | | |
| b. X none of the figures is to be p | | | ± * | |

International Application No PCT/EP2004/006698

| | | | PCT/EP2004/0 | 006698 |
|---|---|---|--------------------------|--|
| ÎPC 7 | SIFICATION OF SUBJECT MATTER C12N5/06 C12N5/10 A61K | 35/34 C12Q1/02 | ? A61P9/0 | 04 |
| According | to International Patent Classification (IPC) or to both national classification | assification and IPC | | |
| | S SEARCHED | | | |
| IPC 7 | documentation searched (classification system followed by class ${\tt C.12N}$ | sification symbols) | | |
| | | | | |
| Document | ation searched other than minimum documentation to the extent | that such documents are includ | ed in the fields search | ed |
| | | | | |
| Electronic | data base consulted during the international search (name of da | ita base and, where practical, s | earch terms used) | |
| EPO-Ir | nternal, BIOSIS, MEDLINE | | | |
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| | ENTS CONSIDERED TO BE RELEVANT | | | |
| Category ° | Citation of document, with indication, where appropriate, of th | e relevant passages | | Relevant to claim No. |
| X | WO 03/010303 A (ES CELL INTL. PTE LTD; NETHERLANDS INSTITUUT VOOR ONTWIKKELINGSBIOGIE) 6 February 2003 (2003-02-06) | | | 1-18, 40-42, 45-50, 62-75, |
| | examples 80,81 | | | |
| X | MUMMERY C ET AL: "Differentiation of human embryonic stem cells to cardiomyocytes: Role of coculture with visceral endoderm-like cells." CIRCULATION, vol. 107, no. 21, 3 June 2003 (2003-06-03), pages 2733-2740, XP008029536 ISSN: 0009-7322 (ISSN print) Published online 12 May 2003 the whole document | | | 1-18, 40-42, 45-50, 62-75, 80,81 |
| | , , , , , , , , , , , , , , , , , , , | -/ | | |
| X Furthe | er documents are listed in the continuation of box C. | χ Patent family mem | bers are listed in annex | |
| O* document referring to an oral disclosure, use, exhibition or other means P* document published prior to the international filing date but later than the priority date claimed | | 'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. '&' document member of the same patent family | | |
| ate of the ac | tual completion of the international search | Date of mailing of the int | emational search repo | rt |
| 17 January 2005 | | 01/02/2005 | | |
| ame and ma | iling address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 | Authorized officer | | |
| | NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Teyssier, B | | |

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International Application No
PCT/EP2004/006698

| C.(Continu | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | PCT/EP2004/006698 |
|------------|--|---------------------------|
| Category ° | | Relevant to claim No. |
| | | Helevalli to claim No. |
| X | WO 02/051987 A (AXIOGENESIS AG) 4 July 2002 (2002-07-04) cited in the application the whole document | 18-20, 45-75, 80,81 |
| x | US 5 733 727 A (FIELD LOREN J) 31 March 1998 (1998-03-31) | 18-20, 43-75, 80,81 |
| | examples 4,5 | , - |
| X | MUELLER M ET AL: "Selection of ventricular-like cardiomyocytes from ES cells in vitro" FASEB JOURNAL, vol. 14, no. 15, December 2000 (2000-12), pages 2540-2548, XP002180458 ISSN: 0892-6638 the whole document | 18-20, 45-75, 80,81 |
| | SPIELMANN H ET AL: "The use of transgenic embryonic stem (ES) cells and molecular markers of differentiation for improving the embryonic stem cell test (EST)" CONGENITAL ANOMALIES, vol. 40, no. Suppl., December 2000 (2000-12), pages S8-S18, XP008029541 ISSN: 0914-3505 the whole document | 45-49, 57-75, 80,81 |
| | KETTENHOFEN R ET AL: "Transgenic murine embryonic stem cells as an in-vitro model for developmental toxicity: An alternative to the gold standard" NAUNYN-SCHMIEDEBERG'S ARCHIVES OF PHARMACOLOGY, vol. 365, no. Supplement 1, March 2002 (2002-03), page R154, XP001189334 43rd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology; Mainz, Germany; 12-14 March 2002 ISSN: 0028-1298 Abstract 601 | 45-49, 57-75, 80,81 |
| | SACHINIDIS A ET AL: "Cardiac specific differentiation of mouse embryonic stem cells." CARDIOVASCULAR RESEARCH, vol. 58, no. 2, 1 May 2003 (2003-05-01), pages 278-291, XP002313488 ISSN: 0008-6363 | |
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| Category • | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | | In the state of the No. | |
| | Citation of document, with indication, where appropriate, of the relevant passages | | Relevant to claim No. | |
| , X | KOLOSSOV E ET AL: "Transplantation of the cardiomyocytes selected from transgenically designed ES cells: Quality control and engrafting support of fibroblasts." TISSUE ENGINEERING, vol. 9, no. 4, August 2003 (2003-08), pages 853-854, XP008029529 Second Meeting of the European Tissue Engineering Society; Genoa, Italy; 3-6 September 2003 ISSN: 1076-3279 (ISSN print) Abstract 230 | | 1-20, 45-75, 80,81 | |
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 17-20 and 50-56 are directed to methods of treatment (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the composition.

Continuation of Box II.2

Claims Nos.: 76-79

(E)

Present claims 76-79 relate to methods of manufacturing a drug where the drug is to be identified by the assay of claims 62-75. Neither support within the meaning of Article 6 PCT nor disclosure within the meaning of Article 5 PCT is provided for any individual drug. A meaningful search over the whole of the claimed scope is impossible, as such "reach-through" claims actually intend to cover an invention that has not yet been made. Consequently, no search has been carried out for claims 76-79 and those parts of claims 80 and 81 which refer to claims 76-79.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

International application No. PCT/EP2004/006698

INTERNATIONAL SEARCH REPORT

| Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet) |
|---|
| This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. X Claims Nos.: 17-20, 50-56 because they relate to subject matter not required to be searched by this Authority, namely: |
| Although claims 17-20 and 50-56 are directed to methods of treatment (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the composition. |
| 2. X Claims Nos.: 76-79 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| see FURTHER INFORMATION sheet PCT/ISA/210 |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet) |
| This International Searching Authority found multiple inventions in this International application, as follows: |
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| 1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. |
| 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| |
| 4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: |
| |
| Remark on Protest The additional search fees were accompanied by the applicant's protest. |
| No protest accompanied the payment of additional search fees. |

Information on patent family members

F. POT #04 P10 /n-1--- 1----

International Application No PCT/EP2004/006698

| | | | | 101/612 | 2004/000098 |
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